

# **APPENDIX A**

## **MARKED-UP VERSION**

**Attorney Docket: 4257.1US**

1. A kit of parts for gene delivery to a recipient cell in a host, using a gene delivery vehicle to which a humoral response can be raised, comprising a nucleic acid comprising a gene to be delivered to said recipient cell and further comprising a second composition of a second gene delivery vehicle essentially identical to said first gene delivery vehicle, but preferably lacking said gene to be delivered.

2. A kit of parts according to claim 1, wherein said second composition is a vaccine and wherein said first composition is a composition for gene therapy.

3. A kit of parts according to claim 2, wherein said vaccine is to be administered at a time before said gene therapy composition at a moment in time sufficient for the host to raise a neutralising humoral response to said second gene delivery vehicle.

4. (Amended) A kit of parts according to [any one of ]claim[s] 1[-3], wherein said second gene delivery vehicle comprises a nucleic acid encoding an indifferent protein.

5. (Amended) A kit of parts according to [any one of ]claim[s] 1[-4], wherein a gene delivery vehicle is of adenoviral origin.

6. (Amended) A kit of parts according to [any one of ]claim[s] 2-5] 1, wherein said gene therapy composition comprises a number of first gene delivery vehicles above the number that can be neutralised by a humoral response of said host.

7. A method for delivering a gene of interest to a recipient cell in a host using a gene delivery vehicle comprising a nucleic acid comprising said gene of interest, said method comprising administering to a host a vaccine composition comprising a gene delivery vehicle lacking said gene to be delivered, allowing for a neutralising humoral response to be raised by said host to said gene delivery vehicle lacking said gene to be delivered and administering a composition for gene therapy comprising essentially the same gene delivery vehicle having a

nucleic acid comprising said gene to be delivered in an amount greater than the amount which can be neutralised by said humoral response.

8. A method for avoiding or diminishing liver toxicity in a host of a gene delivery composition upon administration, comprising administering to a host a vaccine composition comprising a gene delivery vehicle, preferably lacking said gene to be delivered, allowing for a neutralising humoral response to be raised by said host to said gene delivery vehicle lacking preferably said gene to be delivered and administering a composition for gene therapy comprising essentially the same gene delivery vehicle having a nucleic acid comprising said gene to be delivered in an amount greater than the amount which can be neutralised by said humoral response.

9. (Amended) A method according to claim 7[ or 8], wherein said gene delivery vehicle is of adenoviral origin.

10. (Amended) A kit of parts according to [any one of ]claim[s] 1[-6] in the preparation of a pharmaceutical for the use as a pharmaceutical.

11. (Amended) Use of a kit of parts according to [any one of ]claim[s] 1[-6] in the preparation of pharmaceutical for the treatment of diseases associated with uncontrolled proliferation of cells in a host, such as tumors or autoimmune diseases.

12. (Amended) Use of a kit of parts according to [any one of ]claim[s] 1[-6] in the preparation of a pharmaceutical for the treatment of diseases associated with genetic defects in a host.

13. (Amended) A kit of parts according to [any one of ]claim[s] 1[-6], wherein said gene of interest is interleukin-3.

14. (Amended) A method for the preparation of a kit of parts according to [anyone of]claim[s] 1[-6], comprising preparing at least one gene delivery vehicle by inserting a gene of interest in a nucleic acid to be delivered to a host cell, packaging said nucleic acid in a vehicle capable of entering a host cell and bringing a resulting gene delivery vehicle in a medium suitable for administration to a host.

15. A method according to claim 14, wherein said nucleic acid is based on or derived from an adenovirus.

16. (Amended) A method according to claim 14[ or 15], wherein said vehicle comprises adenoviral structural proteins.

17. A method according to claim 16, wherein at least one vehicle comprises proteins from adenoviruses of different serotypes.

18. (Amended) A method according to [any one of]claim[s 15-17]15, wherein said nucleic acid comprises at least one ITR and a packaging signal based on or derived from an adenovirus.

19. (Amended) A method according to [any one of]claim[s 15-18]15, wherein said nucleic acid does not encode functional structural adenoviral proteins.

20. (Amended) A method according to [any one of]claim[s 15-19]15, wherein said nucleic acid encodes E2A adenoviral gene product.

21. A method according to claim 20, wherein said E2A gene product is temperature sensitive.

22. (Amended) A method according to [any one of ]claim[s 14-21]14, wherein said packaging occurs in a packaging cell.

23. A method according to claim 22 wherein said packaging cell is derived from or based on a primary cell.

24. A method according to claim 23, wherein said cell is based on or derived from PER.C6.

25. (Amended) A method according to [any one of ]claim[s 15-18]15 wherein said nucleic acid comprising said gene of interest is produced by a recombination step from two adenoviral vectors.

26. (Amended) A method according to [any one of ]claim[s 15-25]15, wherein said adenovirus is an adenovirus serotype 5 or serotype 35.